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The association between serum uric acid and blood pressure in different age groups in a healthy Chinese cohort

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Abstract

High serum uric acid (sUA) has been reported to be a risk factor for hypertension however, whether this is the case for all age groups is not clear. We examined the association between sUA concentrations and systolic and diastolic blood pressure (SBP and DBP) in different age groups in a cohort of healthy Chinese participants.

A total of 1082 healthy participants aged from 41 to 70 years were included. sUA concentration was measured by the uricase-peroxidase method. SBP and DBP were assessed using mercury sphygmomanometry. Hypertension was defined as SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg. Hyperuricemia (HUA) was defined as sUA concentration of >7 mg/dL in men and >6 mg/dL in women. The association between sUA concentration and SBP and DBP was examined using Pearson's correlation test, multivariate linear regression, and logistic regression analysis.

The prevalence of hypertension and HUA increased with age ($P < .001$). Hypertension was more common in participants that had HUA than in those that did not (38.95% vs 30.16%, $P = .02$). Higher sUA was significantly associated with higher SBP and DBP in the 41- to 50-year-old participants (SBP, $\beta = 0.35$, $P < .001$; DBP, $\beta = .29$, $P < .001$; after adjustment for age, sex, total cholesterol, estimated glomerular filtration rate, and fasting plasma glucose). HUA was also a risk factor for hypertension in this age group (odds ratio 1.425, 95% confidence interval, 1.217–1.668, $P < .001$). There was no association between sUA concentration and SBP and DBP in the other age groups.

In this population of healthy Chinese participants, sUA concentration was positively associated with hypertension only in the 41- to 50-year-old group. Lowering uric acid in this age group may help to reduce the incidence of hypertension.

Abbreviations: DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, HDL-C = high-density lipoprotein-cholesterol, HUA = hyperuricemia, LDL-C = low-density lipoprotein-cholesterol, SBP = systolic blood pressure, sCr = serum creatinine, sUA = serum uric acid, TC = total cholesterol.

Keywords: serum uric acid, hyperuricemia, blood pressure, hypertension

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1. Introduction

The prevalence of hypertension is increasing in many countries, and is an important risk factor for cardiovascular mortality and morbidity.^[1,2] Established risk factors for hypertension include older age, dyslipidemia, and diabetes.^[3] High serum uric acid (sUA) has been reported to be a risk factor for hypertension in some cohorts including participants from a healthy Japanese population.^[4–7] In contrast no association between high sUA and hypertension has been reported in some other cohorts, including those with established type 1 diabetes.^[8,9]

Previous studies suggest that the relation between sUA concentration and blood pressure may vary at different ages.^[10–14] The National Health and Nutrition Examination Survey reported that a sUA concentration of >5.5 mg/dL was associated with a 2-fold greater risk of hypertension, and that for every 0.1 mg/dL increase in sUA concentration, the risk of hypertension was increased by 38% in 12 to 17 years old people.^[10] This relation between sUA concentration and blood pressure was reported to be absent in a cohort of Chinese participants aged 90 to 108 years.^[11] Similarly, it was reported that high sUA concentrations were associated with high blood pressure in Korean participants aged <40 but not ≥ 40 years old,^[12] whereas this association was only present in Japanese participants aged ≥ 40 but not <40 years old.^[14] So it is possible that the relationship between sUA and blood pressure varies at

different ages in different populations.^[13,14] The relationship between sUA and blood pressure at different ages has not, however, been previously studied in a Chinese population. Therefore, in the present study, we aimed to investigate whether high sUA concentration was associated with hypertension in different age groups in a Chinese population.

2. Methods

2.1. Subjects

A total of 1198 subjects who underwent health examinations during March to August 2014 were enrolled from the Health Physical Examination Center of Ganzi Prefecture Hospital, Sichuan Province, China. Subjects (n=110) with a history of taking medications which could affect blood pressure or sUA (including nitrates, corticosteroid, contraceptive pills, antidepressant drugs, and antihypertension drugs) were excluded. Subjects (n=6) with primary liver disease (serum glutamic pyruvic transaminase >80 IU/L) or primary kidney disease (estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m²) were also excluded from the study. The remaining 1082 participants were included in the final analysis. To investigate the effect of age on the association between sUA and blood pressure, subjects were divided into 3 groups according to their age: 41 to 50 (n=362), 51 to 60 (n=360), and 61 to 70 years groups (n=360).

The study was approved by the Research Ethics Committees of Qianfoshan Hospital Affiliated to Shandong University, and Ganzi Autonomous Prefecture Hospital, Sichuan Province. All participants provided written informed consent.

2.2. Baseline measurements and definitions

Blood pressure was measured in all participants by trained professionals using conventional mercury sphygmomanometry. Blood pressure was measured in both arms after the patient rested for 10 minutes and the higher value was regarded as the blood pressure of the patient.^[15] Blood pressure was measured 3 times at 2-minute intervals in all participants and mean SBP and DBP were calculated. Hypertension was defined as SBP ≥140 mm Hg, or DBP ≥90 mm Hg.

Venous blood samples were collected after an overnight fast (≥12 hours). sUA concentrations were measured by the uricase-peroxidase method.^[16] According to the Chinese Expert Consensus on hyperuricemia (HUA) and gout treatment, HUA was defined as sUA concentration of >7 mg/dL in men and >6 mg/dL in women.^[17] The following additional serum biochemical parameters were measured using the Olympus AU2700 automatic biochemical analyzer: glutamic-oxaloacetic transaminase, albumin, total cholesterol (TC), triglyceride, low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), serum creatinine (sCr), and fasting plasma glucose. eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation: $eGFR = 186.3 \times (sCr \text{ in mg/dL})^{-1.154} \times \text{age}^{-0.203} \times 0.827$ (for Chinese) $\times 1$ (for men) or 0.742 (for women).^[18,19]

2.3. Statistical analysis

The data were normally distributed according to the Kolmogorov-Smirnov normality test. All statistical analyses were performed using SPSS version 19.0. Continuous data were presented as mean ± standard deviation. Comparison among means was performed by a one-way ANOVA followed by *Duncan test* post hoc test. The χ^2 test was used to compare the prevalence of hypertension or HUA among different age groups. Correlation was assessed by Pearson's test. Multiple linear regression analysis was used to analyze the contribution of age, sex, TC, eGFR, and fasting plasma glucose to the association of sUA concentration with SBP and DBP, and logistic regression analysis was used to analyze the contribution of these factors to the association of HUA with hypertension. A *P* value of <0.05 was regarded as statistically significant.

3. Results

The baseline characteristics of the 1082 participants were summarized in Table 1. The participants were divided into 3 groups aged 41 to 50 (n=362), 51 to 60 (n=360), and 61 to 70 (n=360) years. The sex ratio, HDL, triglyceride, and glutamic-oxaloacetic transaminase were comparable among these 3 groups (*P* > .05). There was a significant difference among the groups in the following parameters: SBP, DBP, sUA, eGFR, total

Table 1
Baseline characteristics of the participants.

Variables	Total (n=1082)	41–50 y (n=362)	51–60 y (n=360)	61–70 y (n=360)	<i>P</i>
N (male: female)	536:546	181:181	178:182	177:183	>.05
Age, y	55.42 ± 8.60	45.45 ± 2.81*	55.54 ± 2.83*	65.32 ± 2.90*	<.001
SBP, mm Hg	126.23 ± 20.49	121.33 ± 15.64	123.38 ± 18.49	134.30 ± 24.14*	<.001
DBP, mm Hg	79.40 ± 14.33	76.41 ± 12.46	78.31 ± 13.80	83.51 ± 15.63*	<.001
sUA, mg/dL	5.17 ± 1.80	4.90 ± 1.66*	5.26 ± 1.78	5.34 ± 1.93	<.001
eGFR, mL/min/1.73 m ²	99.86 ± 34.81	109.57 ± 40.29*	97.63 ± 34.59*	92.32 ± 25.73*	<.05
TC, mmol/L	4.23 ± 1.13	4.180 ± 1.08	4.20 ± 1.19	4.42 ± 1.10*	<.01
LDL-C, mmol/L	2.78 ± 0.89	2.69 ± 0.81	2.74 ± 0.98	2.90 ± 0.86*	<.01
HDL-C, mmol/L	0.99 ± 0.30	0.99 ± 0.27	0.99 ± 0.32	1.01 ± 0.32	>.05
Triglyceride, mmol/L	1.13 ± 0.81	1.14 ± 0.96	1.11 ± 0.75	1.14 ± 0.69	>.05
FPG, mmol/L	4.74 ± 1.52	4.58 ± 1.40	4.77 ± 1.30	4.88 ± 1.81	<.05
Albumin, g/L	39.30 ± 6.05	40.21 ± 5.62*	39.27 ± 6.29	38.48 ± 6.12	<.001
GOT, IU/L	30.08 ± 23.78	29.56 ± 20.95	31.09 ± 26.52	29.60 ± 23.58	>.05

Comparison among 3 age groups was performed by a one-way ANOVA.

DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, GOT = glutamic-oxaloacetic transaminase, HDL-C = high-density lipoprotein-cholesterol, LDL-C = low-density lipoprotein-cholesterol, N = number, FPG = fasting plasma glucose, SBP = systolic blood pressure, sUA = serum uric acid, TC = total cholesterol.

* *P* < .05, compared with both of the other 2 age groups by post hoc Duncan test.

Table 2**The prevalence of HUA and hypertension in different age groups.**

Variables	Total (n=1082)	41–50 y (n=362)	51–60 y (n=360)	61–70 y (n=360)	P
Hypertension	345 (31.88%)	73 (20.17%)*	107 (29.72%)*	165 (45.83%)*	<.001
HUA	190 (17.56%)	52 (14.36%)	56 (15.56%)	82 (22.78%)*	.006

Comparison among 3 age groups was performed by a one-way ANOVA.

HUA=hyperuricemia.

* $P < .05$, compared with both of the other 2 age groups by post hoc Duncan's test.

cholesterol, LDL-cholesterol, fasting plasma glucose, and albumin (Table 1). The difference in eGFR between any 2 age groups was significant ($P < .05$). SBP, DBP, total cholesterol, LDL-cholesterol of the 61 to 70 years age group were significantly higher than those of the 41 to 50 and 51 to 60 years age groups ($P < .05$). sUA levels of both the 51 to 60 and 61 to 70 years age groups were significantly higher than that of the 41 to 50 years age group ($P < .05$). The fasting plasma glucose level of the 61 to 70 years age group was higher than that of the 41 to 50 years age group ($P < .05$) (Table 1).

The prevalence of hypertension increased with age. The prevalence of hypertension in the 61 to 70 years age group (45.83%) was significantly higher than that in both the 41 to 50 years age group (20.17%, $P < .001$) and the 51 to 60 years age group (29.72%, $P < .001$; Table 2). The prevalence of hypertension in the 51 to 60 years age group (29.72%) was also significantly higher than that in the 41 to 50 years age group (20.17%, $P < .05$; Table 2).

A similar trend was observed for HUA. The prevalence of HUA in the 61 to 70 years age group (22.78%) was significantly higher than that in both the 41 to 50 years age group (14.36%, $P = .006$) and the 51 to 60 years age group (15.56%, $P = .006$).

The prevalence of hypertension in participants with HUA was significantly higher than that of participants with normal uric acid levels (38.95% vs 30.16%, $P < .05$; Fig. 1).

According to the multivariate linear regression analysis, higher sUA was significantly associated with higher SBP in the whole cohort ($\beta = 0.10$, $P = 0.001$; Table 3). Further analysis suggested that sUA concentration was significantly positively associated with both SBP and DBP in the 41 to 50 years age group (SBP, $\beta = 0.35$, $P < 0.001$; DBP, $\beta = 0.29$, $P < .001$; Table 3) after

adjustment for age, sex, TC, eGFR, and fasting plasma glucose but not in other age groups.

Multiple logistic regression analyses suggested that HUA was not significantly associated with hypertension (odds ratio 1.073, 95% confidence interval [CI], 0.989–1.164, $P = .088$; Table 4) in the whole cohort. However, HUA was significantly associated with hypertension in the 41 to 50 years age group (odds ratio 1.425, 95% CI, 1.217–1.668, $P < .001$; Table 4).

4. Discussion

The present study suggested that the relationship between HUA and hypertension is limited to younger participants in a healthy Chinese population with normal blood pressure, sUA, kidney function, and lipid profile. We found this association to be present in participants aged 41 to 50 years but not 51 to 70 years.

A number of epidemiological studies have reported that HUA is accompanied with hypertension.^[20,21] The positive correlation between elevated sUA and hypertension has been described in many populations,^[10,22–25] and increasing amounts of evidence suggests that sUA is a causal contributor to hypertension.^[4,26,27] In a large cohort study involving 2062 participants with a mean follow-up of 21.5 years it was reported that high sUA concentration was independently associated with the incidence of developing hypertension (RR: 1.05, 95% CI, 1.01–1.10, $P = .02$).^[4]

Renal insufficiency^[28] and liver disease^[29] are associated with HUA, and they are also well-established mechanisms for secondary hypertension. We, however, excluded patients with

Table 3**Multivariate linear regression analysis of the association between blood pressure and uric acid.**

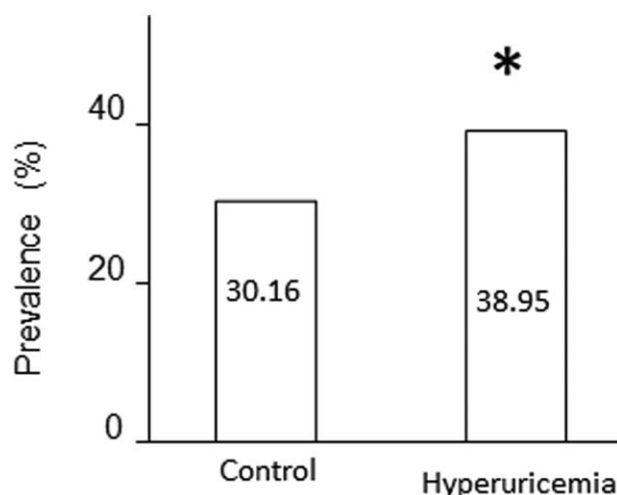
	SBP			DBP		
	β	R^2	P	β	R^2	P
Total	0.10	0.14	.001	0.04	0.11	.22
41–50 y	0.35	0.12	<.001	0.29	0.08	<.001
51–60 y	0.05	0.10	.38	0.03	0.15	.57
61–70 y	0.07	0.08	.20	0.03	0.05	.59

Age, sex, total cholesterol, glomerular filtration rate, and fasting plasma glucose were adjusted for. DBP=diastolic blood pressure, SBP=systolic blood pressure.

Table 4**Multivariate logistic regression analysis of the association between hyperuricemia and hypertension in different age groups.**

Groups	OR	CI	P
Total	1.073	0.989–1.164	.088
41–50 y	1.425	1.217–1.668	<.001
51–60 y	0.959	0.822–1.119	.599
61–70 y	1.056	0.941–1.185	.355

Age, sex, total cholesterol, glomerular filtration rate, and fasting plasma glucose were adjusted for. CI=confidence interval, OR=odds ratio.

**Figure 1.** The prevalence of hypertension in participants that had hyperuricemia and those with normal uric acid levels. $P < .05$.

renal impairment (eGFR < 60 mL/min/1.73 m²) and liver disease (serum glutamic pyruvic transaminase > 80 IU/L). Therefore, the association between HUA and hypertension in the present study is not due to renal insufficiency or liver disease.

Our study suggested that with aging, the incidence of hypertension in the 61 to 70 years age group was 2.27 times higher than that in the 61 to 70 years age group. Only in the 41 to 50 years age group, there was a significant correlation between sUA and blood pressure. Our observation that age affected the correlation between sUA and blood pressure is consistent with some previous reports.^[12] A significant association between sUA and blood pressure was reported in Korean adults aged <60 years but not those aged >60 years for example.^[12] The exact mechanism for the age-related relationship between sUA and blood pressure is still unknown. Whether the age relationship between sUA and blood pressure is due to the difference in ethnicity, certain single-nucleotide polymorphisms, body mass index,^[30] or oxidative oxygen species^[31] needs to be further studied.

It has been reported that sUA is a consistent cardiovascular risk factor in different populations^[32–35] and suggested that lowering sUA with allopurinol may reduce cardiovascular events.^[36,37] It is likely that sUA promotes cardiovascular risk but multiple mechanisms including those unrelated to hypertension such as causing endothelial dysfunction,^[38] increasing oxidative stress,^[39] and inducing renal arteriolopathy.^[40,41] As a result monitoring and lowering sUA levels may be helpful in decreasing cardiovascular events in all age groups, although this remains to be definitely demonstrated.

This study has several limitations. First, its cross-sectional design precludes any causal relationships between UA and hypertension being assumed. Second, the blood pressure in the participants was relatively low and therefore the results should not be extrapolated to populations with higher blood pressure. Third, the participants were all Chinese and whether the findings are similar in other ethnicities needs to be further investigated. Fourth, we adjusted for a variety of important confounding variables of hypertension including age, sex, TC, eGFR, and fasting plasma glucose. However, we did not have information about smoking or physical activity which may affect blood pressure. Residual confounding likely remains.

5. Conclusions

Our data suggest that age affects the correlation between sUA and blood pressure. sUA was positively associated with blood pressure in the 41 to 50 years age group, but not in older participants. Lowering sUA in younger Chinese adults may be helpful in reducing the incidence of hypertension although this remains to be proven.

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